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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/039,956	10/23/2001	Melissa K. Carpenter	091/009C	1602
22869	7590	08/10/2004	EXAMINER	
GERON CORPORATION 230 CONSTITUTION DRIVE MENLO PARK, CA 94025			TON, THAIAN N	
			ART UNIT	PAPER NUMBER

1632

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

24-

Office Action Summary

Application No.

10/039,956

Applicant(s)

CARPENTER ET AL.

Examiner

Ton Thai-An

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 May 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 16 and 37-62 is/are pending in the application.
- 4a) Of the above claim(s) 1 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 16 and 37-62 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Applicants' Amendment, filed 5/24/04, has been entered. Claims 16, 37 and 38 have been amended. Claims 53-62 have been added. Claims 2-15 and 17-36 are cancelled. Claim 1 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected groups, there being no allowable generic or linking claim. Election was made **without** traverse in the paper filed on October 23, 2003. Claims 16 and 37-62 are under current examination.

Priority

Applicants' Amendment to the specification is found to be proper has been entered.

Claim Objections

The prior objections of claims 16 and 40 are withdrawn in view of Applicants' arguments and/or amendment(s) to the claims.

Specification

The amendment filed 5/24/04 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

The amendment which adds the priority claim in the first line of the specification recites that each application 'it is also recognized that.....' is new matter because the amendment was not present and thus, not part of the original disclosure. There is no support for what the synthetic mixture is, or what combination of derived factors that are known to be beneficial..... Therefore, the attempt to incorporate the entirety of the information from the priority documents as recited by the new amendment is considered new matter because this was not part of the original disclosure. See MPEP 608.04.

Applicant is required to cancel the new matter in the reply to this Office Action.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The prior rejection of claims 16, 37, 40, 42, 45-50 and 52 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34 and 47 of copending Application No. 09/888,309 is withdrawn in view of Applicants' Arguments.

With regard to the prior rejections of certain of the instant claims (16, 37, 40, 42, 43, 44-50 and 52 in the application under the judicially created doctrine of obviousness type double patenting (for Application Nos. 10/157,288, 10/087,473, 10/087,142, 10/313,739, 10/189,276), Applicants state that because the prosecution of the present application is further advanced than that of the Applications named in the prior Office Action, Applicants argue that the invention claimed in the present application is to be patented before those stated in the prior Office Action. Thus, Applicants undertake to address the double patenting issue appropriately upon determination that claims in the present application, and 10/087,142 are otherwise patentable. See p. 8 of Applicants' response.

Applicants' arguments have been considered, but are not persuasive because the arguments fail to overcome the prior rejections of record because they fail to specifically address how the conflicting claims are not patentably distinct from the claims of the instant invention. Thus, the prior rejections are maintained for reasons of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior rejection of record is maintained. Claims 16 and 17-52 and newly added claims 53-62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of screening a substance, comprising a) obtaining a culture of undifferentiated pPS cells proliferating on an extracellular matrix and in the presence of fibroblast-conditioned medium, wherein the culture is essentially free of feeder cells, b) causing or permitting the pPS cells to differentiate; then c) combining the cells with the substance; and d) determining the phenotypic or metabolic effect of the substance on the cells and methods of screening undifferentiated, pluripotent human ES [hES] cells utilizing undifferentiated hES cells proliferating on an extracellular matrix and in the presence of fibroblast-conditioned medium; does not reasonably provide enablement for the methods of screening a substance comprising contacting a differentiated cell with a substance and determining any phenotypic or metabolic changes that result in the cell from contact with the compound, wherein the differentiated cell is produced by obtaining a culture of undifferentiated pPS cells proliferating in a growth environment that is essentially free of feeder cells and optionally causing or permitting the pPS cells to differentiate, and methods of screening undifferentiated

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hES cells utilizing hES cells proliferating on an extracellular matrix, as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants argue that Lim [cited in the prior Office action] does not undermine the patentability of the invention claimed and demonstrates the inventive nature because Lim assumes that all the complex interactions provided by feeder cells are required for hES cells to be grown. Applicants argue that the present disclosure shows the effects obtained by the direct contact with the feeder cells can be replaced with contact with extracellular matrix components, and that a relatively uncomplicated nutrient medium can provide all the other all other support required for undifferentiated cell growth and that the feeder-free culture system of the present invention is elegant in its simplicity because it defies the conventional teaching in the ES cell art. Applicants further argue that the growth conditions selected for the working examples, such as the medium used are not critical features of the new feeder-free culture method described and enabled by the instant invention. Applicants argue that See pp.8-9 of Applicants' Response.

Applicants' arguments are not persuasive. The teachings of the present invention do not defy conventional teaching in the ES cell art because the art teaches that ES cells require fibroblasts (or unidentified factors isolated from fibroblasts) to maintain the cells in an undifferentiated state. The prior Office

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action addresses the requirement for both an extracellular matrix and fibroblast-conditioned medium to maintain the hES cells in an undifferentiated state. Clearly, the instant specification supports this by stating that “[T]he role of the feeder cells is replaced by supporting the culture (of pPS cells) on an extracellular matrix and culturing the cells in a conditioned medium.” See p. 3, lines 29-31. Applicants have overcome the prior rejection in part by amending the instant claims to recite the proliferation of the undifferentiated hES cells on an extracellular matrix. However, it is maintained that the state of the art teaches the unpredictability in culturing ES cells in an undifferentiated state, and Lim supports this by teaching that specific factors which would be required for supporting undifferentiated growth of hES cells have yet to be identified in medium isolated from fibroblasts. Thus, Lim supports that fibroblast-conditioned medium provide factors which support undifferentiated growth of hES cells. The state of the art teaches that ES cells that are grown in the absence of fibroblast cells die, and the instant specification supports this by showing that only fibroblast-conditioned medium, and is thus a critical feature of the culture system, is able to support undifferentiated growth of hES cells. The specification fails to provide teachings or guidance with regard to growing hES cells in an undifferentiated state with any type of medium, as encompassed by the claims. Accordingly, it is maintained that the pPS and hES cells of the invention would need to be grown on an extracellular matrix and with a

fibroblast-conditioned medium in order to maintain the cells in an undifferentiated state.

Applicants argue that aspects of the culture system referred to in the prior Office action are not considered critical to the invention because the detailed description teaches key elements of the medium, such as the usual components to enhance cell survival, including isotonic buffer, essential minerals and either serum or serum replacement. Applicants argue that at the time the application was filed, conditioned medium was a preferred embodiment of the invention. See p. 10 of the Response. Applicants argue that some of the cell lines used to condition the medium represent an embodiment of the invention, and that such cell lines can be identified by testing, and other suitable cells that may have features that are characteristic of fibroblasts, or cells such as mesenchymal cells. Applicants argue that by employing the culture test system and marker assessment protocol provide by the specification, synthetically assemble media can be used and assessed to identify effective combinations of culture environment components and that it would be unfair to limit applicant to culture conditions exemplified in the working examples. See pp. 10-11 of the Response.

This is not persuasive. Applicants have failed to provide any particular teaching or guidance with regard to medium, other than fibroblast conditioned medium, that when used as described would maintained hES cells (or pPS cells) in an undifferentiated state. Applicants do not provide any specific teaching or

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guidance for other cells, such as mesenchymal cells, to be used to condition medium to maintain undifferentiated hES cells. The mere recitation of the use of cells such as mesenchymal cells is not sufficient to overcome the unpredictability taught by the art of record, and the teachings provided by the instant specification, which show that non-fibroblast conditioned medium [made from hTERT-RPE] fail to maintain undifferentiated growth of hES cells.

Applicants state that scientists at Geron have demonstrated human ES cells can readily grow in fresh medium with added growth factors, and point to X-VIVO™ and QBSF-60™ which Applicants claim have been tested and found useful as suitable base nutrient medium. See p. 11 of the Response.

This is not persuasive. The arguments of counsel cannot take the place of evidence in the record. See *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965) and MPEP §716.01. Applicants have not provided an appropriate affidavit or declaration supporting that medium other than fibroblast-conditioned medium, can support undifferentiated growth of hES (and pPS) cells. Without such an affidavit or declaration, the Examiner cannot ascertain the ability of other medium to support undifferentiated growth of hES cells; for example, what growth factors, or other factors, that are contained in the medium. Accordingly, the prior rejection is maintained for reasons of record.

Claim Rejections - 35 USC § 112

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The prior rejection of claim 37 and 39 are withdrawn in view of Applicants' amendments to the claims.

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Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the Examiner be unavailable, inquiries should be directed to Amy Nelson, Acting SPE of Art Unit 1632, at (571) 272-0804. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

tnt

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